REMARKS

Amended claims 1, 16, and 53 and new claim 78 specify that the nucleic acid recited in the claims has an internal ribosome entry site. Support for this amendment is found throughout the specification, for example, on page 2, lines 22-26; page 6, lines 17-22; page 23, lines 23-26; page 30, lines 1-17; and page 33, lines 13-18. Claim 61 has been amended to specify that the nucleic acid has a splice acceptor site, as disclosed, for example, on page 2, lines 19 and 20; page 23, lines 17-31; and page 32, line 28 through page 33, line 7. New claims 76 and 77 recite the use of a cassette with a prokaryotic promoter operably linked to a positive selection marker (page 12, lines 5-13, and page 14, lines 17-25).

A marked-up version indicating the amendments made to the claims, as required by 37 C.F.R. § 1.121(c)(1)(ii), is enclosed. No new matter is introduced by any of the amendments.

Enclosed is a check for \$27.00 for the excess claims fee. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

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Art Unit:

2899

Serial No.:

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Examiner:

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October 25, 2001

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COMPOSITIONS AND METHODS FOR THE DISCOVERY AND

SELECTION OF BIOLOGICAL INFORMATION

Commissioner For Patents Washington, D.C. 20231

Version with Markings to Show Changes Made

A marked-up versions of claims 1, 16, 53, and 61 and new claims 76-78 are presented below.

- 1. (Amended) A method of selecting for one or more cells having a specific response to a stimulatory agent of interest, said method including the steps of:
- (a) inserting a vector including a cassette comprising <u>an internal ribosome</u> <u>entry site</u>, a positive selection marker, a negative selection marker, and a reporter gene into eukaryotic cells under conditions that result in the integration of said cassette into the genome of said cells, whereby said reporter gene is operably linked to a regulatory element in at least one cell; and

- (b) selecting cells in which expression of said reporter gene is specifically activated by said stimulatory agent.
- 16. (Amended) A method of selecting for one or more cells having a specific response to a stimulatory agent of interest, said method including the steps of:
- (a) inserting a vector including a cassette comprising <u>an internal ribosome</u> <u>entry site</u>, a positive selection marker, a negative selection marker, and a reporter gene into eukaryotic cells under conditions that result in integration of said cassette into the genome of said cells, whereby said reporter gene is operably linked to a regulatory element in at least one cell; and
- (b) selecting cells in which expression of said reporter gene is specifically inactivated by said stimulatory agent.
- 53. (Amended) A nucleic acid including <u>an internal ribosome entry site</u>, a positive selection marker, a negative selection marker, and a reporter gene.
- 61. (Amended) A nucleic acid including a splice acceptor site, a positive selection marker, a negative selection marker, and a recombinase signal sequence.

Add the following new claims 76-78.

- 76. (New) The method of claim 1, wherein said cassette further comprises a prokaryotic promoter operably linked to said positive selection marker.
- 77. (New) The method of claim 16, wherein said cassette further comprises a prokaryotic promoter operably linked to said positive selection marker.

78. (New) The method of claim 51, wherein said cassette further comprises an internal ribosome entry site.

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